

WHAT IS CLAIMED IS:

1. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group consisting of:
- (a) a nucleotide sequence encoding the full-length DR4 polypeptide having the complete amino acid sequence in Figure 1 (SEQ ID NO:2), including the predicted leader sequence;
 - (b) nucleotide sequence encoding the full-length DR4 polypeptide having the complete amino acid sequence in Figure 1 (SEQ ID NO:2), including the predicted leader sequence but lacking the amino terminal methionine;
 - (c) a nucleotide sequence encoding the mature DR4 polypeptide (full-length polypeptide with the leader removed) having the amino acid sequence at positions about 24 to about 468 in Figure 1 (SEQ ID NO:2);
 - (d) a nucleotide sequence encoding the full-length DR4 polypeptide having the complete amino acid sequence including the leader encoded by the cDNA clone contained in ATCC Deposit No. 97853;
 - (e) a nucleotide sequence encoding the full-length DR4 polypeptide having the complete amino acid sequence including the leader but lacking the amino terminal methionine encoded by the cDNA clone contained in ATCC Deposit No. 97853;
 - (f) a nucleotide sequence encoding the mature DR4 polypeptide having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97853;
 - (g) a nucleotide sequence that encodes the DR4 extracellular domain having the amino acid sequence at positions about 24 to about 238 of SEQ ID NO:2, or as encoded by ATCC Deposit No. 97853;
 - (h) a nucleotide sequence that encodes the DR4 transmembrane domain having the amino acid sequence at positions about 239 to about 264 of SEQ ID NO:2, or as encoded by ATCC Deposit No. 97853;
 - (i) a nucleotide sequence that encodes the DR4 intracellular domain having the amino acid sequence at positions about 265 to about 468 of SEQ ID NO:2, or as encoded by ATCC Deposit No. 97853;
 - (j) a nucleotide sequence that encodes the DR4 death domain having the amino acid sequence at positions about 379 to about 422 of SEQ ID NO:2, or as encoded by ATCC Deposit No. 97853; and
 - (k) a nucleotide sequence complementary to any of the nucleotide sequences in (a), (b), (c), (d), (e), (f), (g), (h), (i), or (j) above.

118

2. The nucleic acid molecule of claim 1 wherein said polynucleotide has the complete nucleotide sequence in Figure 1 (SEQ ID NO:1).

5 3. The nucleic acid molecule of claim 1 wherein said polynucleotide has the nucleotide sequence in Figure 1 (SEQ ID NO:1) encoding the DR4 polypeptide having the amino acid sequence in positions 2 - 468 of SEQ ID NO:2.

10 4. The nucleic acid molecule of claim 1 wherein said polynucleotide has the nucleotide sequence in Figure 1 (SEQ ID NO:1) encoding the extracellular domain of the DR4 polypeptide having the amino acid sequence from about 24 to about 238 in SEQ ID NO:2.

5. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group consisting of:

- 5 (a) a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of residues n-468 of SEQ ID NO:2, where n is an integer in the range of 1-109;
- 10 (b) a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of residues 1-m of SEQ ID NO:2, where m is an integer in the range of 221 - 468;
- 15 (c) a nucleotide sequence encoding a polypeptide having the amino acid sequence consisting of residues n-m of SEQ ID NO:2, where n and m are integers as defined respectively in (a) and (b) above; and
- 20 (d) a nucleotide sequence encoding a polypeptide consisting of a portion of the complete DR4 amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97853 wherein said portion excludes from 1 to about 108 amino acids from the amino terminus of said complete amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97853;
- 25 (e) a nucleotide sequence encoding a polypeptide consisting of a portion of the complete DR4 amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97853 wherein said portion excludes from 1 to about 249 amino acids from the carboxy terminus of said complete amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97853; and
- 30 (f) a nucleotide sequence encoding a polypeptide consisting of a portion of the complete DR4 amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97853 wherein said portion include a combination of any of the amino terminal and carboxy terminal deletions in (d) and (e), above.

6. The nucleic acid molecule of claim 1 wherein said polynucleotide has the complete nucleotide sequence of the cDNA clone contained in ATCC Deposit No. 97853.

7. The nucleic acid molecule of claim 1 wherein said polynucleotide has the nucleotide sequence encoding the DR4 polypeptide having the complete amino acid sequence excepting the N-terminal methionine encoded by the cDNA clone contained in ATCC Deposit No. 97853.

8. The nucleic acid molecule of claim 1 wherein said polynucleotide has the nucleotide sequence encoding the extracellular domain of the DR4 polypeptide having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97853.

5

9. An isolated nucleic acid molecule comprising a polynucleotide which hybridizes under stringent hybridization conditions to a polynucleotide having a nucleotide sequence identical to a nucleotide sequence in (a), (b), (c), (d), (e), (f), (g), (h), (i), (j) or (k) of claim 1 wherein said polynucleotide which hybridizes does not hybridize under stringent hybridization conditions to a polynucleotide having a nucleotide sequence consisting of only A residues or of only T residues.

10

10. An isolated nucleic acid molecule comprising a polynucleotide which encodes the amino acid sequence of an epitope-bearing portion of a DR4 polypeptide having an amino acid sequence in (a), (b), (c), (d), (e), (f), (g), (h), (i), (j) or (k) of claim 1.

15

11. The isolated nucleic acid molecule of claim 10, which encodes an epitope-bearing portion of a DR4 polypeptide wherein the amino acid sequence of said portion is selected from the group consisting of: a polypeptide comprising amino acid residues from about 35 to about 92 of SEQ ID NO:2, a polypeptide comprising amino acid residues from about 114 to about 160 of SEQ ID NO:2, a polypeptide comprising amino acid residues from about 169 to about 240 of SEQ ID NO:2, a polypeptide comprising amino acid residues from about 267 to about 298 of SEQ ID NO:2, a polypeptide comprising amino acid residues from about 330 to about 364 of SEQ ID NO:2, a polypeptide comprising amino acid residues from about 391 to about 404 of SEQ ID NO:2, and a polypeptide comprising amino acid residues from about 418 to about 465 of SEQ ID NO:2.

25

30

12. A method for making a recombinant vector comprising inserting an isolated nucleic acid molecule of claim 1 into a vector.

35

13. A recombinant vector produced by the method of claim 12.

35

14. A method of making a recombinant host cell comprising introducing the recombinant vector of claim 13 into a host cell.

15. A recombinant host cell produced by the method of claim 14.

16. A recombinant method for producing a DR4 polypeptide, comprising culturing the recombinant host cell of claim 15 under conditions such that said polypeptide is expressed and recovering said polypeptide.

5

17. An isolated DR4 polypeptide comprising an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:

10 (a) the amino acid sequence of the full-length DR4 polypeptide having the complete amino acid sequence in Figure 1 (SEQ ID NO:2), including the predicted leader sequence;

15 (b) the amino acid sequence of the full-length DR4 polypeptide having the complete amino acid sequence in Figure 1 (SEQ ID NO:2), including the predicted leader sequence but lacking the amino terminal methionine;

20 (c) the amino acid sequence of the mature DR4 polypeptide (full-length polypeptide with the leader removed) having the amino acid sequence at positions about 24 to about 468 in Figure 1 (SEQ ID NO:2);

25 (d) the amino acid sequence of the full-length DR4 polypeptide having the complete amino acid sequence including the leader encoded by the cDNA clone contained in ATCC Deposit No. 97853;

30 (e) the amino acid sequence of the full-length DR4 polypeptide having the complete amino acid sequence including the leader but lacking the amino terminal methionine encoded by the cDNA clone contained in ATCC Deposit No. 97853;

(f) the amino acid sequence of the mature DR4 polypeptide having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97853;

35 (g) the amino acid sequence of the DR4 extracellular domain having the amino acid sequence at positions about 24 to about 238 of SEQ ID NO:2, or as encoded by ATCC Deposit No. 97853;

(h) the amino acid sequence of the DR4 transmembrane domain having the amino acid sequence at positions about 239 to about 264 of SEQ ID NO:2, or as encoded by ATCC Deposit No. 97853;

(i) the amino acid sequence of the DR4 intracellular domain having the amino acid sequence at positions about 265 to about 468 of SEQ ID NO:2, or as encoded by ATCC Deposit No. 97853; and

35 (j) the amino acid sequence of the DR4 death domain having the amino acid sequence at positions about 379 to about 422 of SEQ ID NO:2, or as encoded by ATCC Deposit No. 97853.

18. An isolated polypeptide comprising an epitope-bearing portion of
the DR4 protein, wherein said portion is selected from the group consisting of: a
polypeptide comprising amino acid residues from about 35 to about 92 of SEQ ID
NO:2, a polypeptide comprising amino acid residues from about 114 to about 160
of SEQ ID NO:2, a polypeptide comprising amino acid residues from about 169 to
about 240 of SEQ ID NO:2, a polypeptide comprising amino acid residues from
about 267 to about 298 of SEQ ID NO:2, a polypeptide comprising amino acid
residues from about 330 to about 364 of SEQ ID NO:2, a polypeptide comprising
amino acid residues from about 391 to about 404 of SEQ ID NO:2, and a
polypeptide comprising amino acid residues from about 418 to about 465 of SEQ
ID NO:2.

19. An isolated antibody that binds specifically to a DR4 polypeptide of
claim 17.

20. An isolated nucleic acid molecule comprising a polynucleotide
encoding a DR4 polypeptide wherein, except for at least one conservative amino
acid substitution, said polypeptide has a sequence selected from the group
consisting of:

(a) a nucleotide sequence encoding the full-length DR4 polypeptide having
the complete amino acid sequence in Figure 1 (SEQ ID NO:2), including the
predicted leader sequence;

(b) nucleotide sequence encoding the full-length DR4 polypeptide having
the complete amino acid sequence in Figure 1 (SEQ ID NO:2), including the
predicted leader sequence but lacking the amino terminal methionine;

(c) a nucleotide sequence encoding the mature DR4 polypeptide (full-length
polypeptide with the leader removed) having the amino acid sequence at positions
about 24 to about 468 in Figure 1 (SEQ ID NO:2);

(d) a nucleotide sequence encoding the full-length DR4 polypeptide having
the complete amino acid sequence including the leader encoded by the cDNA clone
contained in ATCC Deposit No. 97853;

(e) a nucleotide sequence encoding the full-length DR4 polypeptide having
the complete amino acid sequence including the leader but lacking the amino
terminal methionine encoded by the cDNA clone contained in ATCC Deposit No.
97853;

(f) a nucleotide sequence encoding the mature DR4 polypeptide having the
amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No.
97853;

(g) a nucleotide sequence that encodes the DR4 extracellular domain having the amino acid sequence at positions about 24 to about 238 of SEQ ID NO:2, or as encoded by ATCC Deposit No. 97853;

5 (h) a nucleotide sequence that encodes the DR4 transmembrane domain having the amino acid sequence at positions about 239 to about 264 of SEQ ID NO:2, or as encoded by ATCC Deposit No. 97853;

10 (i) a nucleotide sequence that encodes the DR4 intracellular domain having the amino acid sequence at positions about 265 to about 468 of SEQ ID NO:2, or as encoded by ATCC Deposit No. 97853;

15 (j) a nucleotide sequence that encodes the DR4 death domain domain having the amino acid sequence at positions about 379 to about 422 of SEQ ID NO:2, or as encoded by ATCC Deposit No. 97853; and

15 (k) a nucleotide sequence complementary to any of the nucleotide sequences in (a), (b), (c), (d), (e), (f), (g), (h), (i), or (j) above.

21. An isolated DR4 polypeptide wherein, except for at least one conservative amino acid substitution, said polypeptide has a sequence selected from the group consisting of:

20 (a) the amino acid sequence of the full-length DR4 polypeptide having the complete amino acid sequence in Figure 1 (SEQ ID NO:2), including the predicted leader sequence;

25 (b) the amino acid sequence of the full-length DR4 polypeptide having the complete amino acid sequence in Figure 1 (SEQ ID NO:2), including the predicted leader sequence but lacking the amino terminal methionine;

30 (c) the amino acid sequence of the mature DR4 polypeptide (full-length polypeptide with the leader removed) having the amino acid sequence at positions about 24 to about 468 in Figure 1 (SEQ ID NO:2);

(d) the amino acid sequence of the full-length DR4 polypeptide having the complete amino acid sequence including the leader encoded by the cDNA clone contained in ATCC Deposit No. 97853;

35 (e) the amino acid sequence of the full-length DR4 polypeptide having the complete amino acid sequence including the leader but lacking the amino terminal methionine encoded by the cDNA clone contained in ATCC Deposit No. 97853;

(f) the amino acid sequence of the mature DR4 polypeptide having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97853;

35 (g) the amino acid sequence of the DR4 extracellular domain having the amino acid sequence at positions about 24 to about 238 of SEQ ID NO:2, or as encoded by ATCC Deposit No. 97853;

(h) the amino acid sequence of the DR4 transmembrane domain having the amino acid sequence at positions about 239 to about 264 of SEQ ID NO:2, or as encoded by ATCC Deposit No. 97853;

5 (i) the amino acid sequence of the DR4 intracellular domain having the amino acid sequence at positions about 265 to about 468 of SEQ ID NO:2, or as encoded by ATCC Deposit No. 97853, and

(j) the amino acid sequence of the DR4 death domain having the amino acid sequence at positions about 379 to about 422 of SEQ ID NO:2, or as encoded by ATCC Deposit No. 97853.

add a7

add E

add C7